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On Some New Quinazoline Derivatives

DISSERTATION

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIRE-
MENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY,
IN THE FACULTY OF PURE SCIENCE OF COLUMBIA
UNIVERSITY

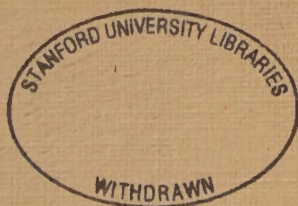
BY

ROSS AIKEN GORTNER, B.Sc., M.A.,
NEW YORK CITY

1909

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ACKNOWLEDGMENT.

The nature and general scope of the work embodied in this dissertation were suggested to me in the fall of 1908 by Professor Marston Taylor Bogert, and the investigation has been carried out under his direction.

The author wishes to take this opportunity of thanking him for his interest in the work, his thoughtful advice and the encouragement which was given in moments when failure seemed imminent.

The writer also wishes to thank Dr. Nelson and Dr. Hoffman of the Organic Laboratories for advice and favors received.

R. A. G.

ORGANIC LABORATORY,
HAVEMEYER HALL,
COLUMBIA UNIVERSITY,
April, 1909.

Inscribed as a slight token of my regard to my first Pro-
fessor of Chemistry,
FREDERICK JAMES ALWAY.

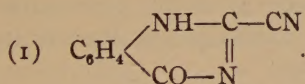
HISTORICAL.

The Amino Quinazolines.

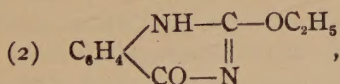
In 1869¹ Griess treated an alcoholic solution of anthranilic acid with cyanogen and obtained a compound melting at 173° and soluble in alcohol and ether to which he ascribes the composition $C_{10}H_{10}N_2O_2$.

Upon treating the above compound with alcoholic ammonia in a sealed tube at 100° he obtained a different compound crystallizing "in mother-of-pearl flakes" to which the composition $C_8H_7N_3O$ is assigned (no melting point or data of analysis given) and to which he gives the name "Benzkreatinin."

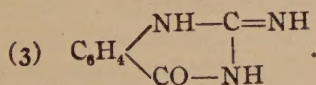
Later,² by treating anthranilic acid in water solution with cyanogen gas, he obtained a compound of the formula $C_9H_5N_3O$, to which he assigns the graphic structure:



From this structure he reasons that the compound $C_{10}H_{10}N_2O_2$ obtained in alcoholic solution has the structure:

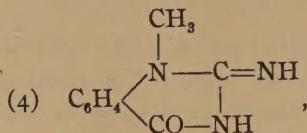


and that on heating this with ammonia the ethoxy group is broken off, giving an imide:



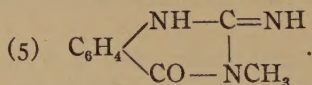
In a still later paper³ (1880) he obtains the $C_8H_7N_3O$ compound by the action of cyanamide upon an aqueous solu-

tion of anthranilic acid and again gives formula (3), calling the compound "Benzylcocyamidin." By treatment with methyl iodide he obtained a compound to which he gives the structure



and which he calls "ortho methyl benzglycocyamidin."

He also treats the ethoxy compound (2) with methyl amine and obtains "B. ortho methyl Benzglycoamidin" to which formula (5) is ascribed:



His work has been repeated in part by the author and the results are given on page 41 of this dissertation.

The next work on amino-quinazolines is reported by Paul and Neuberger,⁴ in 1893.

By the action of *m*-nitro anilin on *o*-nitrobenzyl chloride in the presence of formic acid they were able to obtain *o*-nitrobenzoylformyl-*m*-nitranilin, which, on reduction, gave *3-meta-amidophenyldihydroquinazoline*, melting at 147°.

By reduction of the dihydroquinazoline with metallic sodium in alcoholic solution the *tetrahydro* compound was obtained melting at 156°.

In a later paper⁵ Paal and Kromschröder describe *3-ortho-amidophenyldihydroquinazoline*, which is made in a similar manner to the meta derivative by substituting orthonitranilin. The dihydroamidoquinazoline melts at 165° and "acts as a strong base."

Still later⁶ Paal and Poller describe the paraamidophenyl derivative, which was made in an analogous manner to the

ortho and meta derivatives. The dihydro compound melting at 175° and the tetrahydro derivative at 138° .

In 1895 St. von Niemontowski⁷ describes a monoamino and a diamino derivative of *2,4-dioxy-7-methylquinazoline*. These amino derivatives were prepared by reducing the nitration products, the position of the nitro groups being unknown, although the author states that the dinitro compound is "probably either 5.8 or 6.8." The monoamino melts at 308° and the diamino decomposes at 333° .

The next work in this field was done by Busch, Birk and Lehrmann⁸ in 1897.

They prepared *3-orthoamidobenzyl-2-thiotetrahydroquinazoline* by boiling orthodiaminodibenzylamine with carbon disulphide in the presence of alkali. The compound shows all the amino properties and melts at 212° . By reducing the above compound with sodium they were able to prepare *3-orthoaminobenzyltetrahydroquinazoline*, melting at $88-89^{\circ}$.

2-Phenyl-3-orthoamidobenzyltetrahydroquinazoline was obtained from benzaldehyde condensed with orthodiamidodibenzylamine. The amino compound formed melts at 140° and is decomposed into benzaldehyde and the original base by treatment with dilute acids.

By substituting salicylic aldehyde and paraoxybenzaldehyde for the benzaldehyde the authors were able to obtain respectively:

2-Orthooxyphenyl-3-amidobenzyltetrahydroquinazoline, melting at 166° , and *2-paraoxyphenyl-3-amidobenzyltetrahydroquinazoline*, melting at 90° . Both of these compounds are easily broken down into their original components by dilute acids.

Wheeler, Johnson and McFarland,⁹ in 1903, prepared *2-amino-3-phenyl-4-ketodihydroquinazoline* by treating the 2-chlor derivative with ammonia in a sealed tube at $120-130^{\circ}$. The compound is described as "colorless prisms melting at $237-238^{\circ}$ and forming on boiling with dilute hydrochloric acid, *2,4-diketo-3-phenyltetrahydroquinazoline*."

Kunczell¹⁰ states that by treating 2,4-diketotetrahydroquinazoline with hydrazine hydrate he was able to prepare 2,4-diketo-3-aminotetrahydroquinazoline, melting at 269°–270°. No properties or data of analysis are given.

Thode,²⁵ in 1904, prepared 3-*N*-amino-4-ketodihydroquinazoline by treating *o*-amidobenzhydrazid with the theoretical quantity of glacial formic acid and heating to boiling. The cooled mass solidified and on recrystallization from alcohol melted at 204°. Condensations and analysis are reported with benzaldehyde and salicylaldehyde. The phenylamido derivative was obtained and the fact that by action of nitrous acid the *N*-amino group was replaced by hydrogen was noted.

Kratz²⁶ had previously prepared a nitro derivative of Thode's *N* amino quinazoline by the action of anhydrous formic acid upon *m*-nitro *o*-amido benzhydrazid. This 3-*N*-amino-4-keto-7-nitrodihydroquinazoline was reported on melting at 170–171° and, aside from analysis, was not farther investigated.

Bogert and Cook²⁷ prepared 6-nitro-2-methyl-3-*N*-amino-4-ketodihydroquinazoline by the action of hydrazine hydrate upon 5-nitro acetanthranil. The quinazoline melts at 208–209°.

The corresponding 7-nitro-2-methyl-3-*N*-amino-4-ketodihydroquinazoline was later prepared in an analogous manner by Bogert and Klaber²⁸ by treating 4-nitro acetanthranil with hydrazin hydrate. The compound melts at 223° and pours both a monoacetyl and a diacetyl derivative.

In 1906, Bogert and Chambers¹¹ prepared 5-amino-4-ketodihydroquinazoline by the reduction of a corresponding nitro compound. The amino body melts at 235–236°, and possesses all the amino properties. Various addition products are described.

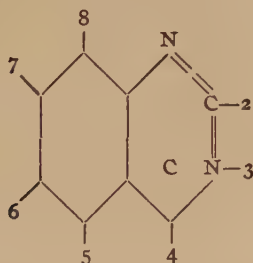
The authors also described 2-methyl-4-keto-5-aminodihydroquinazoline, which was obtained by reducing the corresponding nitro body. The aminoquinazoline melts at 295–310° with decomposition.

In a later paper Bogert and Seil¹² describe the preparation

of *2-methyl-3-N-amino-4-keto-5-nitrodihydroquinazoline* from 5-nitroacetanthrananil and hydrazine hydrate. The amino derivative melts at 152–3° and forms the usual amino addition products.

Theoretical and Introduction.

Of the twenty-three amino bodies described under historical, only thirteen can be classed as true amino quinazolines, *i. e.*, compounds in which the amino group is attached to the quinazoline nucleus. Of these thirteen compounds four are miazine derivatives of amino benzol and the remaining nine are benzo derivatives of aminomiazines, in six of which the amino is attached to an *N* (position 3) of the heterocycle and in the other three instances attached to the carbon in position 2.



According to the position of this amino group the properties are changed to a considerable extent.

While the *C*-aminos have been known for many years, it was not until 1900 that Buch and Heinrichs¹³ prepared the first *N*-amino by condensing α,β -dicarboxylphenylhydrazine

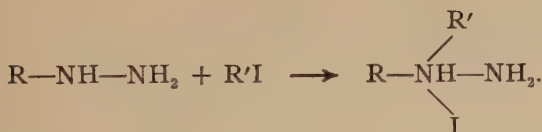
Reagent.	Secondary hydrazine group.	N-Amino group.	C-Amino group.	Aromatic.
Mineral acids	Salts	Salts	Salts	Salts
Nitrous acid	Nitrosamine	Amino group replaced by hydro-gen	Amino replaced by hydroxyl	Diazo bodies
Chloroform and alkali	Isocyanide	Isocyanide(?) In some instances no odor is obtained	Isocyanide	Isocyanide
Acetic anhydride	Acetylates	Monoacetyl**	Acetylates	Acetylates to di-acetyl
Ketones	Combines readily	If combination, with great difficulty	Combines readily	Combines readily
Aldehydes	Combines readily	No combination with aliphatic	Combines readily	Combines readily
Oxidation	By HgO to tetrazones	Not affected	Not affected	Oxidized to quinones
Methyl iodide	Quaternary azonium compounds	Azonium compounds do not form. Will not methylate	Azonium compounds, methylates	Methylates
Aromatic nitroso		No change		Azo bodies
Phenyl mustard oil	Phenyl thio-semicarbazones	Phenyl thio-semicarbazones	Phenyl thio-semicarbazones	Phenyl thio-semicarbazones
Phenyl isocyanate	Combines readily to semicarbazids	Combines with great difficulty.*	Combines to phenyl uramino	Combines to phenyl uramino

* Franzen¹⁴ states that no combination occurs but I have obtained a condensation with 2-methyl-3-N-amino-4-keto-dihydroquinazoline and phenyl isocyanate.

** When a nitro group is in position 5 of the quinazoline nucleus the N-amino in position 3 gives a diacetyl derivative.

with hydrazine forming a urazin derivative. It was found that while this amino group was in some respects similar to a *C*-amino it also had hydrazin characteristics to a small extent and beside these possessed peculiar properties of its own. In later work Franzen¹⁴ and Bulow¹⁵ independently undertook researches on *N*-amino compounds and from their work, as well as my own investigations, I have prepared the following table showing the properties of *C*-amino groups, *N*-amino groups and hydrazine groups. By a comparison of these classes it will be seen that a great difference is possible in the two types of amino quinazolines. The reactions have been tabulated as near as possible in order of importance, judging from the aromatic chemistry rather than the aliphatic series.

From the above table it will be seen that the *C*-amino group is much more reactive than an *N*-amino, the reactivity of the *N*-amino being less than the secondary hydrazins to which it is so closely allied. This may be explained by the fact that the usual additions which hydrazins undergo are additions on the α -nitrogen atom,¹⁶ thus with methyl iodide we get an addition,



When, therefore, this nitrogen is bound up in a heterocycle its properties are very much altered. While this investigation was originally intended to be concerned only with amino derivatives of the quinazolines it was later found advisable to prepare various other substituted quinazolines, although anything bearing directly on the amino bodies was given priority.

In general, the amino bodies investigated behaved as might

be expected from the foregoing table and served to confirm the results already obtained.

SOME CONDENSATIONS OF ACETANTHRANIL AND THE OXAL ANTHRANILS.

The experimental work on these condensations has been classed in what seems a logical sequence to the author and is therefore divided into:

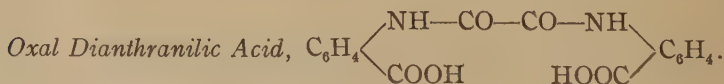
1. The preparation of anthranils.
2. The condensations of acetanthranil.
3. The condensations of ethyl- and methyloxalanthranils.
4. The condensations of oxal dianthranil.
5. Other condensations.

EXPERIMENTAL.

1. The Preparation of Anthranils.

Acetantranilic Acid.—On boiling anthranilic acid with acetic anhydride for a short time with return condenser and allowing to cool, crystals of acetantranilic acid separated, melting at 185° , corrected. These were similar in properties to those found by Bedson and King.¹⁶

Acetantranil.—On boiling anthranilic acid for some minutes in an open vessel it is converted into acetantranil. There is a considerable loss in the reaction, due to the formation of acetamide, etc. (Best yield 89% theory.) Acetantranil has been described by Bredt and Hof.¹⁷ It crystallized in yellow needles, carrying no anhydride of crystallization or in large prisms carrying anhydride of crystallization. The anhydrous needles melt at $79-80^{\circ}$ (cor.). On recrystallization from aqueous solvents or even from 95% alcohol, it takes up water and is quantitatively converted into acetantranilic acid.



—This compound had already been prepared by Mauthner and Suida.¹⁸ They describe it as a "white, insoluble powder, not melting below 280°," and give the following analysis, which seems to be somewhat low, but probably due to the difficulties experienced in purifying an insoluble compound, although they dissolved in ammonia and precipitated it with sulphuric acid.

	Calc. Per cent.	Found. Per cent.	Found. Per cent.
Carbon	58.53	58.11	57.95
Hydrogen	3.66	4.03	3.68
Nitrogen	8.54	9.18	

For this work the acid was prepared by three methods:

1. As originally prepared by heating a mixture of 1 molecule oxal diethyl ester with 2 molecules anthranilic acid in an oil bath at 140° for some time. The crude mass was then extracted with hot water and washed with dilute alcohol.

2. One molecule of methyl oxal ester and 2 of anthranilic acid were heated together in an oil bath from 150°–155° for 30 minutes, the solid mass was extracted with water and washed with dilute alcohol.

3. Treated 5 grams anthranilic acid in anhydrous benzol with 4 grams oxalyl chloride (boiling point 62°–64°). A violent reaction took place and fumes of hydrochloric acid were given off. The precipitated residue was filtered and washed with benzol and alcohol.

From each of these methods a white powder was obtained decomposing at 330° (uncorr.) and corresponding in properties to those already found by Mauthner and Suida¹⁸ and from the method of preparation there can be little doubt as to the formula. When freshly prepared from methyl oxalate it is appreciably soluble in alcohol, but soon becomes insoluble on standing.

Oxal Dianthranil, $\text{C}_6\text{H}_4 \begin{array}{c} \diagup \text{N} \text{---} \text{CO} \text{---} \text{CO} \text{---} \text{N} \diagdown \\ | \qquad \qquad | \\ \text{CO} \qquad \qquad \text{CO} \end{array} \text{C}_6\text{H}_4$. — Five grams oxaldianthranilic acid was heated to boiling with an

excess of acetic anhydride for three hours, using return condenser. The compound changed from a white to a yellow on boiling and after cooling the mixture was filtered and the solid washed with acetic anhydride. Yield 3.4 grams.

Oxal dianthranil is a yellow powder which is insoluble in all ordinary organic solvents and melting at 345° with decomposition. On boiling with water for a short time it is not hydrolyzed, but long boiling hydrolyzes it to the acid.

For analysis the crude product was again boiled with acetic anhydride for three hours, washed with acetic anhydride, and dried at 110° .

0.1670 gram substance gave 14.8 cc. nitrogen at 24° and 763 mm.

(1) 0.1901 gram substance gave 0.4545 gram CO_2 and 0.0513 gram H_2O .

(2) 0.1691 gram substance gave 0.4029 gram CO_2 and 0.0433 gram H_2O .

(3) 0.1898 gram substance gave 0.4581 gram CO_2 and 0.0516 gram H_2O .

	Calculated for $\text{C}_{16}\text{H}_8\text{N}_2\text{O}_4$	Per cent.	Found. Per cent.	Per cent.
N	9.59	9.98	...	...
C	65.75	65.20	64.97	65.81
H	2.74	3.02	2.87	3.05



—Equimolecular proportions of methyl oxalate and anthranilic acid were intimately mixed and heated in an oil bath at 140° – 155° for 30 minutes. The mixture quickly fused and methyl alcohol vapors were given off. After 30 minutes heating the mass had solidified in the bottom of the flask. The flask was broken and the cake ground up in a mortar with water, filtered, and washed. The residue was extracted with dilute alcohol and the filtrates combined and concentrated. On cooling crystals separated which on recrystallization from

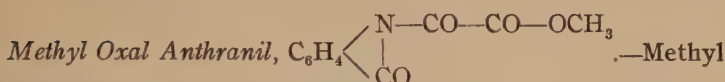
hot water melted at 176.5° (corr.). The compound is soluble in hot water, alcohol, benzol, and alkalis; insoluble in chloroform or ligroin. It dissolves readily in cold sodium carbonate solution with evolution of CO_2 .

In the preparation of this acid some of the oxal dianthranilic acid was formed.

For analysis the acid was recrystallized from a mixture of alcohol and benzol, washed with ligroin, and dried at 110° .

0.1115 gram gave 5.8 cc. nitrogen at 17° and 766 mm.

	Calculated for $\text{C}_{10}\text{H}_9\text{O}_6\text{N}$. Per cent.	Found. Per cent.
Nitrogen	6.27	6.17

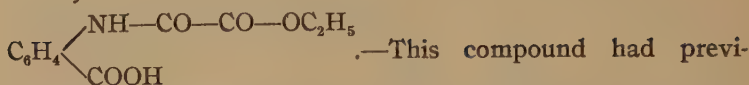


oxalanthranilic acid was heated to boiling for some minutes with an excess of acetic anhydride. The excess of anhydride was carefully evaporated and the residue allowed to cool. The mass of crystals thus obtained was pressed out on a porous plate and dried. Recrystallized from dry benzol they melted constant on first recrystallization at 177.5° (corr.). That it was not the mother substance is proven by the fact that when mixed with methyl oxalanthranilic acid the mixture melted at 150° (uncorr.).

Methyl oxalanthranil crystallizes from acetic anhydride or dry benzol in light brown needles. It is very sensitive to moisture and even in so-called "absolute alcohol" takes up water and is reconverted into methyl oxalanthranilic acid. For analysis it was crystallized from benzol which had been dried over sodium.

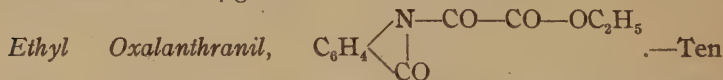
0.2431 gram gave 14.8 cc. nitrogen at 20° and 767 mm.

	Calculated for $\text{C}_{10}\text{H}_7\text{O}_4\text{N}$. Per cent.	Found. Per cent.
Nitrogen	6.83	7.02

Ethyl Oxalanthranilic Acid,

ously been prepared by Baeyer¹⁹ by the oxidation of indoxyl acid ether, and by Mauthner and Suida.¹⁸ It may be prepared in good yield from anthranilic acid and ethyl oxalate.

Twenty grams of anthranilic acid were added to a slight monomolecular excess of ethyl oxalate in a flask and the whole heated in an oil bath to 140–150° for an hour. The mixture at first melted and ethyl alcohol vapors were given off. At the end of an hour all reaction had apparently ceased and the mass had solidified. The temperature was then raised to 160° for ten minutes and then allowed to cool. The solid was extracted with boiling water to separate any insoluble oxal dianthranilic acid. On cooling the solutions white needles of ethyl oxalanthranilic acid separated, melting sharply at 184° (corr.). Yield 70 per cent. theory. Yield of oxal dianthranilic acid 1.4 grams.



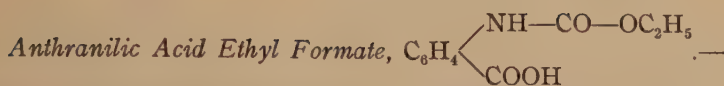
grams of ethyl oxalanthranilic acid were dissolved in boiling acetic anhydride in excess and the solution evaporated to a small bulk. On cooling large white flakes separated, which were filtered off and dried on a porous plate. Upon recrystallization from acetic anhydride they melt sharply at 129–30° (corr.). Yield 81 per cent. theory.

Ethyl oxalanthranil in contrast to the methyl ester is not easily hydrolyzed and may be recrystallized from dilute alcohol without hydrolysis. On boiling with water, however, it is readily converted into the acid.

For analysis the compound was recrystallized from acetic anhydride and dried at 110°.

0.3509 gram gave 20.4 cc. nitrogen at 20.5° and 765 mm.

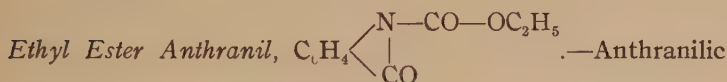
	Calculated for $C_{11}H_9O_4N$. Per cent.	Found. Per cent.
Nitrogen	6.40	6.67



Five grams anthranilic acid was treated with an excess of ethyl chlor formate and the mixture heated to boiling. After boiling for a few minutes the mixture was filtered and the solid was washed with water and recrystallized from dilute alcohol. In this manner long, coarse, stellate groups of needles were obtained insoluble in water, very soluble in alcohol, and melting at 125.5° (corr.). The compound is readily soluble in dilute sodium carbonate solution.

0.2733 gram gave 16.6 cc. nitrogen at 24° and 762 mm.

	Calculated for $C_{10}H_{11}O_4N$. Per cent.	Found. Per cent.
Nitrogen	6.69	6.83



acid ethyl formate was dissolved in hot acetic anhydride and evaporated in an oil bath to almost dryness. Upon cooling the mass solidified. This was redissolved and again taken down to almost dryness. The mass so obtained deposited small white crystals which were dried on a porous plate and lastly in a desiccator over sulphuric acid and solid KOH. Melting point 82° (corr.).

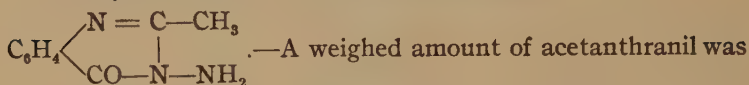
The anthranil is easily hydrolyzed by water and is very soluble in acetic anhydride. It was difficultly obtained in a crystalline form, due to the extreme ease of solubility in all substances which would not hydrolyze it.

0.3225 gram gave 21.4 cc. nitrogen at 24° and 764 mm.

	Calculated for $C_{10}H_9O_3N$. Per cent.	Found. Per cent.
Nitrogen	7.33	7.48

II. Condensations of Acetantrhranil.

2-Methyl 3-Amino 4-Keto Dihydroquinazoline,



added with stirring to a slight molecular excess of hydrazine hydrate in aqueous solution. Heat was developed by the reaction and a white solid separated. This was dissolved by heating to boiling and upon cooling long white needles separated containing 1 molecule of water of crystallization.

2-Methyl, 3-amino, 4-keto dihydroquinazoline is very soluble in almost all organic solvents, but is most easily recrystallized from dilute alcohol. It loses the water of crystallization at 90–100° and the anhydrous base then at 152° (corr.) to a colorless liquid. Yield, almost quantitative.

0.9046 gram gave 0.0860 gram water at 110°.

	Calculated for $\text{C}_9\text{H}_9\text{ON}_3 \cdot \text{H}_2\text{O}$. Per cent.	Found. Per cent.
Water	9.32	9.50

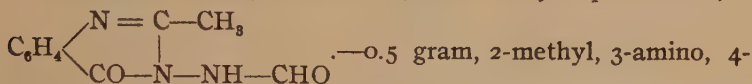
0.1200 gram anhydrous quinazoline gave 25.4 cc. nitrogen at 21° and 759 mm.

	Calculated for $\text{C}_9\text{H}_9\text{ON}_3$. Per cent.	Found. Per cent.
Nitrogen	24.00	24.06

Hydrochloride of 2-Methyl, 3-Amino, 4-Keto Dihydroquinazoline.

To a saturated aqueous solution of the amino quinazoline concentrated hydrochloric acid was added. A white precipitate was thrown down which recrystallized from dilute hydrochloric acid in long needles, melting at 206.9° (corr.). The hydrochloride is readily soluble in water and is not hydrolyzed by boiling.

2-Methyl, 3-Formyl, amino, 4-Keto Dihydroquinazoline,

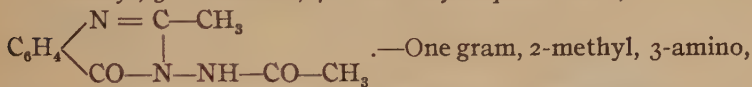


keto dihydroquinazoline was treated with an excess of glacial formic acid and evaporated to dryness. The residue was dissolved in chloroform and precipitated with benzol. Redissolved and again precipitated. The formyl derivative is very soluble in water, alcohol and acetic acid; readily soluble in chloroform and only slightly soluble in benzol. Upon recrystallization from chloroform it may be obtained in the form of long gray needles, which become soft at 185° and melt at $203-04^\circ$ (corr.).

0.1050 gram gave 18.4 cc. nitrogen at 18° and 770 mm.

	Calculated for $\text{C}_{10}\text{H}_9\text{O}_2\text{N}_3$. Per cent.	Found. Per cent.
Nitrogen	20.68	20.52

2-Methyl, 3-Acetamino, 4-Keto Dihydroquinazoline,



4-keto dihydroquinazoline was treated with an excess of acetic anhydride and heated to boiling. Upon evaporating the excess of acetic anhydride and allowing the residue to cool a clear glass remained. This was soluble in hot water, glacial acetic acid, alcohol and benzol, but separated from all except benzol in a resinous condition. From benzol crystals were obtained in the form of short prisms containing benzol of crystallization. The benzol was very quickly lost on exposure to the air and the crystals then disintegrate. When pure the compound melts at 176.5° (corr.).

For analysis the freshly crystallized substance was quickly dried by pressing between filter papers and after weighing dried to constant weight at 100° . The weight was constant after ten minutes' heating.

0.4272 gram gave 0.0672 gram benzol lost.

	Calculated for (C ₁₁ H ₁₁ O ₂ N ₃) ₂ .C ₆ H ₆ . Per cent.	Found. Per cent.
Benzol	15.23	15.73

0.1630 gram dry substance gave 27.6 cc. nitrogen at 22° and 766 mm.

	Calculated for C ₁₁ H ₁₁ O ₂ N ₃ . Per cent.	Found. Per cent.
Nitrogen	19.35	19.33

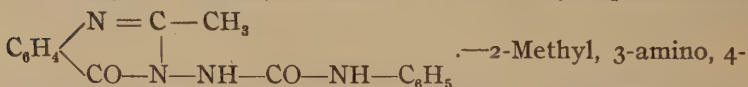
Picrate of 2-Methyl, 3-Amino, 4-Keto Dihydroquinazoline.

0.5 gram of the amino quinazoline was dissolved in 95 per cent. alcohol and added to a warm solution of 0.7 gram picric acid in alcohol. In a few seconds a bright yellow crystalline precipitate was thrown down which was filtered off, washed with water, and dried at 110°. Yield 90 per cent. theory. The picrate is sparingly soluble in water and in alcohol, blackens at 187° (corr.) and dyes wool and silk a bright yellow.

0.1514 gram gave 27.6 cc. nitrogen at 20° and 766 mm.

	Calculated for C ₁₅ H ₁₂ O ₈ N ₆ . Per cent.	Found. Per cent.
Nitrogen	20.78	21.01

2-Methyl, 3-Phenyluramino, 4-Keto Dihydroquinazoline,



keto dihydroquinazoline was treated with an excess of phenyl isocyanate and the mixture heated for an hour in an oil bath at 150–60°. After about 40 minutes heating a crystalline solid began to separate and after the hours' heating the mass was almost solid. This solid was then allowed to cool, extracted and washed with ether to eliminate any unchanged phenyl isocyanate. The white residue was then extracted with hot alcohol, washed on the filter with hot alcohol, and dried at 110°. Yield almost quantitative.

The phenyluramino derivative forms a white crystalline powder, not melting below 300° and insoluble in water, alcohol,

acetone, benzol, ether, amyl alcohol, and all ordinary organic solvents.

0.1271 gram gave 20.4 cc. nitrogen at 19° and 776 mm.

	Calculated for $C_{16}H_{14}O_2N_4$ Per cent.	Found. Per cent.
Nitrogen	19.04	18.84

2-Methyl, 3-Aminobenzylidene, 4-Keto Dihydroquinazoline,

$$\begin{array}{c}
 \text{C}_6\text{H}_5 \begin{cases} \text{N} = \text{C} - \text{CH}_3 \\ \text{CO} - \text{N} - \text{N} = \text{CH} - \text{C}_6\text{H}_5 \end{cases}
 \end{array}$$
 .—One gram of 2-methyl, 3-amino, 4-keto dihydroquinazoline was boiled for several minutes with an excess of benzaldehyde, water was split out as was shown by cracking. On cooling a considerable volume of alcohol was added and the solution allowed to stand some hours. The benzylidene derivative crystallizes from this alcoholic solution in stellate groups of white needles insoluble in water, sparingly soluble in alcohol, and melting at 183° (corr.). For analysis they were recrystallized from alcohol and dried at 110°.

0.0706 gram gave 10.2 cc. nitrogen at 22° and 747 mm.

	Calculated for $C_{16}H_{13}ON_3$ Per cent.	Found. Per cent.
Nitrogen	15.97	16.08

Action of Nitrous Acid on 2-Methyl, 3-Amino, 4-Keto Dihydroquinazoline.

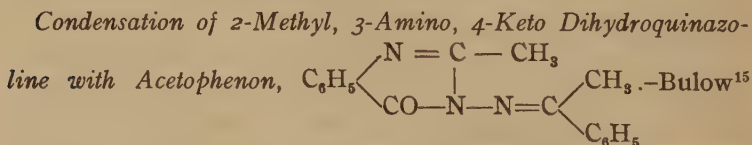
One gram of the amino quinazoline was dissolved in glacial acetic acid, some hydrochloric acid added, and cooled to zero. A 5 per cent. solution of sodium nitrite was then added in calculated quantity and at once a white precipitate was thrown down. This was filtered off and washed with alcohol in which it was slightly soluble. When confined it decomposes at 338° and on strong heating in a shallow dish sublimes undecomposed. Yield 0.9 gram. It recrystallizes from strong hydrochloric acid in needles, insoluble in organic solvents, but very soluble in water. Corresponding in properties to the hydrochloride of 2-methyl, 4-keto dihydroquinazoline.²⁰

0.1615 gram gave 20.6 cc. nitrogen at 18° and 747 mm.

	Calculated for $C_9H_9ON_2.HCl$. Per cent.	Found. Per cent.
Nitrogen	14.25	14.47



This compound has been described by Anschütz, Schmidt, and Greiffenberg,²¹ and was prepared from acetanthranil and ammonia. Prepared by three methods I found identical properties to those mentioned by the above authors. It may be prepared from the hydrochloride described above by just neutralizing with ammonia and evaporating into a small bulk when the free quinazoline crystallizes out. It was also prepared from 2-methyl, 3-amino, 4-keto dihydroquinazoline in a manner similar to the preparation of the hydrochloride. One gram of the amino quinazoline was dissolved in glacial acetic acid and cooled to zero. To this was added a calculated quantity of sodium nitrite solution in small portions. The solution was then heated to boiling and evaporated into small bulk. On cooling crystals were obtained, which upon recrystallization from water, melted at 235° (uncorr.). Yield 0.6 gram. When acetanthranil is added to an alcoholic solution of ammonia the same quinazoline is obtained.



states that when an amino group is attached to an N of a heterocycle condensations may be made with ketones in the manner indicated above.

One gram, 2-methyl, 3-amino, 4-keto dihydroquinazoline was treated with 0.7 gram acetophenon dissolved in absolute alcohol and boiled with return condenser for six hours. 0.9 gram unchanged amino quinazoline was recovered from this solution.

One gram of the amino quinazoline was then treated with 0.7 gram acetophenon and absolute alcohol in small quantity in a sealed tube at 180–200° for nine hours, and the amino quinazoline was recovered unchanged. It would thus appear that in this instance the condensation will not take place.

Dyes Derived from 2-Methyl, 3-Amino, 4-Keto Dihydroquinazoline.

When 2-methyl, 3-amino, 4-keto dihydroquinazoline is treated with nitrous acid no intermediate diazo compound is apparently formed, the reaction apparently going instantly to 2-methyl 4-keto dihydroquinazoline, the amino group being replaced by hydrogen (see page 23). If, on the other hand, this treatment with nitrous acid be carried out under certain conditions a dye may be obtained which is very powerful in tinctorial qualities. That this is not azo dye is shown by analysis.

2-Methyl, 3-Amino, 4-Keto Dihydroquinazoline and β -Naphthol.

1.5 grams of the N-amino quinazoline was dissolved in dilute hydrochloric acid and cooled to + 10°. Into this solution was poured the calculated quantity of sodium nitrite solution. Instantly there was a violent reaction, the solution frothing at the top of the beaker. This frothing solution was *quickly* poured into 1.2 grams β -naphthol dissolved in sodium hydrate solution. The mixture became deep red in color and the dye was precipitated as a dense, red, flocculent powder. This was filtered and washed with water in which it was only sparingly soluble in the cold. The dye was dissolved in concentrated sulphuric acid, in which it is easily soluble to a deep purple color and water added to precipitate the free base. This was filtered, washed with water, and recrystallized in alcohol.

The free base crystallizes in bright red needles which gradually deepen in color from 200–230° and are then so dark that it is difficult to say whether or not they are melted.

They decompose sharply at 266° (corr.), are soluble in alcohol, amyl alcohol, glacial acetic acid, and benzol; insoluble in water; soluble in concentrated mineral acids to intensely colored solutions; dissolve slightly in alkalies to form alkaline salts; the salts are very insoluble in cold water, (ammonium salt soluble 1 part in 15,000 parts of cold water). But even in this dilute solution silk and wool are dyed a deep orange, which is not changed by alkali, acid, or exposure to the light for a considerable period. For analysis the dye was washed with water and alcohol, redissolved in strong sulphuric acid, precipitated with water, washed with water, recrystallized from alcohol and dried at 110° .

0.1293 gram gave 10.8 cc. nitrogen at 17° and 762 mm.

(1) 0.1409 grams gave 0.0570 gram H_2O and 0.3529 gram CO_2 .

(2) 0.1143 gram gave 0.0447 gram H_2O and 0.2859 gram CO_2

	Per cent.	Found.	Per cent
N	9.70		
C	68.30		68.25
H	4.53		4.38

2-Methyl-3-amino-4-ketodihydroquinazoline and α -naphthol.—The treatment with nitrous acid and condensation were carried out in this instance the same as above substituting α -naphthol for β -naphthol. The purification was also accomplished as described above. The salts of the α -derivative are much more soluble than those of the β , and the yield of the solid dye is therefore much smaller. The free base is a brick-red powder, melting with decomposition at 245° (corr.). It dissolves in concentrated sulphuric acid to a deep purple color, is very soluble in alcohol and acetic acid, and insoluble in water. In alkaline or acetic acid solution it dyes silk or wool a rich salmon color.

Efforts were made to prepare other dyes by substituting sulphanilic acid, β -naphthol disulpho acid R, and α -naphthol amino sulpho acids for the α - or β -naphthol but in no case was a dye obtained, although an intense red coloration was produced with 2-amino-6-sulpho-8- α -naphthol, but this product had no dyeing property. In the case of the α - and β -naphthol dyes the tinctorial power is so intense that an amount exceeding 0.5 gram of the dye for 100 gram of fibre would mean a waste of dye, as the maximum strength of solution that will be exhausted is 0.5 per cent. of the weight of the fibre taken. Although no mordant is necessary the operation may be very much hastened by moistening the substance to be dyed in a solution of potassium alum.

On one occasion in carrying out the preparation of the dye as above, a body was obtained which was entirely different in properties from the dye, and which had no appreciable dyeing power.

15 grams 2-methyl-3-amino-4-keto dihydroquinazoline was dissolved in dilute hydrochloric acid and cooled. The calculated quantity of sodium nitrite was then added and the frothing mixture poured at once into 1.2 grams β -naphthol dissolved in KOH. A mass of red crystals separated which were filtered and washed with cold water in which they are slightly soluble. This did not contain potassium. Yield 0.9 grams.

The compound was easily purified by dissolving in 95 per cent. alcohol in small volume and precipitating with water. It is thus obtained in bright orange needles, melting at 144–145° (corr.), very soluble in alcohol, acetone, amyl alcohol, benzol, acetic acid, and caustic alkali. Only slightly soluble in water or dilute mineral acids, and possesses a strong odor of β -naphthol. All further attempts to prepare the compound in larger quantities failed, the dyestuff above described being obtained.

From the analysis it appears to be one molecule of 2-methyl-

4-keto-dihydroquinazoline combined with one molecule of β -naphthol. In what manner the combination has taken place is unknown, but possibly it may be a case of naphthol of crystallization.

0.1537 gram gave 12.4 cc. nitrogen at 18.5° and 754 mm.

(1) 0.1000 gram gave 0.2762 gram CO_2 and 0.0460 gram H_2O .

(2) 0.1173 gram gave 0.3219 gram CO_2 and 0.0557 gram H_2O .

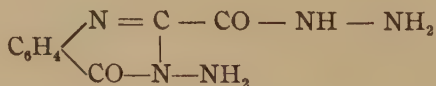
	Calculated for $\text{C}_9\text{H}_8\text{ON}_2 \cdot \text{C}_{10}\text{H}_8\text{O}$.	Found. Per cent.	Per cent.
C	75.00	75.32	74.86
H	5.26	5.11	5.24
N	9.21	9.22	

Owing to the inability to prepare larger quantities the above assumption as to the structure of the compound could not be proven.

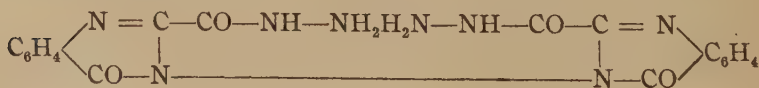
III. The Condensations of the Methyl and Ethyl Oxalanthranils.

Condensation of Ethyl Oxalanthranil with Hydrazin Hydrate.—When either methyl or ethyl oxalanthranil is treated with hydrazine hydrate there are three different combinations possible:

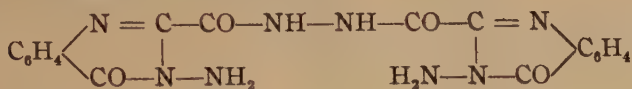
(a) A primary N-amino in position 3 and a hydrazine group replacing the ester group of position 2, giving a product of the formula



(b) Or, the hydrazine group may remain in position 2, and instead of the N-amino in position 3, we may have a diquinazolonyl of the type



(c) Or, the third possibility, in which the N-amino group is found and the two molecules are united through the hydrazine group in position 2, thus giving



That the reaction which does take place is of type (c) is shown by hydrolysis of the resulting compound, a compound of the (a) structure being produced.

Two grams of hydrazine hydrate solution (50 per cent.) were dissolved in 95 per cent. alcohol and two grams of ethyl oxalanthranil slowly added with stirring. The solution was then heated to boiling and the compound not going into solution became a light yellow in color. This was filtered and the yellow filtrate allowed to crystallize from which a yellow amorphous mass was deposited identical with the solid product and only slightly soluble in organic solvents and melting at $157-158^\circ$ (corr.) with loss of ammonia. The melting point was not altered on recrystallization. Total yield 2.1 grams. The same compound was obtained when methyloxalanthranil was substituted for the ethyl ester. For analysis the compound was recrystallized from absolute alcohol and dried at 110° .

0.1132 gram substance gave 27.4 cc. Nitrogen at 19° and 763 mm.

	Calculated for $\text{C}_{18}\text{H}_{14}\text{O}_4\text{N}_8$. Per cent.	Found. Per cent.
Nitrogen	27.60	27.91

All efforts to prepare an acetyl derivative were fruitless as the thick syrup so obtained could not be crystallized and no method of purification could be found.

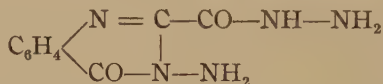
Hydrochloride of 2-Carbazino-3-amino-4-keto Dihydroquinazoline.—One gram ethyl oxalanthranil was added to a solution of 0.5 gram hydrazine hydrate in 95 per cent. alcohol and the

mixture raised to boiling on a water bath. The double compound previously described separated, without filtering concentrated hydrochloric acid was added, and the mixture again boiled. On cooling this was filtered by suction and the white hydrochloride washed on the filter with 95 per cent. alcohol and dried at 110° . Yield 0.8 gram. The hydrochloride is freely soluble in water, but insoluble in alcohol or organic solvents. It crystallizes from strong hydrochloric acid in white needles melting at $190-191^{\circ}$ (corr.) and containing 3 molecules of hydrochloric acid. For analysis it was recrystallized from a mixture of dilute hydrochloric acid and alcohol, washed with alcohol and dried at 110° .

0.1430 gram gave 27.6 cc. Nitrogen at 22° and 764 mm.

	Calculated for $C_8H_8O_2N_6 \cdot 3HCl$ Per cent.	Found. Per cent.
Nitrogen	21.43	21.97

2-Carbazino-3-amino-4-keto-dihydroquinazoline,



1.2 gram of the above hydrochloride was dissolved in a small quantity of water and KOH solution added to alkalinity. Acetic acid was then added to acid reaction and the white precipitate so obtained filtered off and washed with water. It was then recrystallized from dilute alcohol, acidified with acetic acid. On the second recrystallization it separated in beautiful transparent plates, carrying water of crystallization which is lost at $100-110^{\circ}$, the crystals becoming opaque, melting again at 202.5° (corr.).

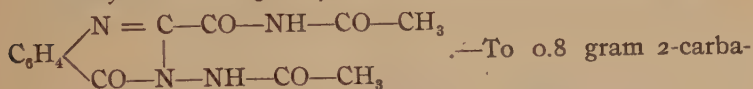
2-Carbazino-3-amino-4-keto-dihydroquinazoline is very soluble in alcohol and quite appreciably soluble in water. When once in solution it is almost impossible to cause it to separate again and when it does crystallize there is always obtained a small portion in an amorphous condition and the loss on re-

crystallization is very great. Less than 0.2 gram were obtained from 1.2 grams of the hydrochloride.

0.1179 gram gave 32 cc. Nitrogen at 18° and 768 mm.

	Calculated for $C_9H_9O_2N_5$ Per cent.	Found. Per cent.
Nitrogen	31.96	31.70

2-Acetyl-carbazino-3-acetylamino-4-keto-dihydroquinazoline,



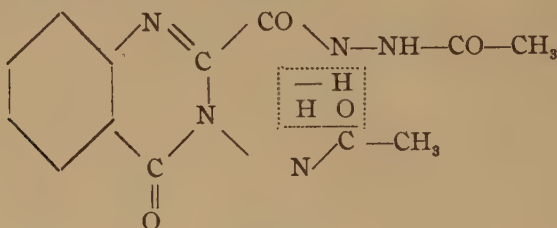
zino-3-amino-4-keto-dihydroquinazoline hydrochloride and 0.6 gram fused sodium acetate was added an excess of acetic anhydride and the mixture evaporated to a small bulk. More acetic anhydride was then added and the insoluble sodium chloride filtered off. The filtrate was twice more evaporated to a small bulk with acetic anhydride, water added, and the evaporation continued to dryness on a water bath. The residue (a clear amber glass) was dissolved in 95 per cent. alcohol, further evaporated to a small bulk, and upon the addition of benzol to this solution the diacetyl compound was precipitated as a fine, yellowish tinted powder. This was filtered off and washed with benzol in which it is almost insoluble. Yield 0.35 gram.

The acetyl derivative forms when pure small transparent plates melt at 125° (corr.). When a small portion is dissolved in benzol upon long boiling they separate again containing benzol of crystallization, but not enough was so obtained on account of the insolubility of the compound to determine the amount of the benzol of crystallization present. The compound is very soluble in water, alcohol and chloroform, separating on evaporating off the solvent as a clear glass. No good crystallizing medium could be found.

0.0715 gram gave 14.20 cc. nitrogen at 16° and 764 mm.

Nitrogen	Calculated for $C_{13}H_{13}O_4N_5$ Per cent.	Found: Per cent.
	23.10	23.16

If from the above 2-acetyl-carbazino-3-acetyl-amino-4-keto-dihydroquinazoline a molecule of water could be eliminated as shown by the graphic formula,

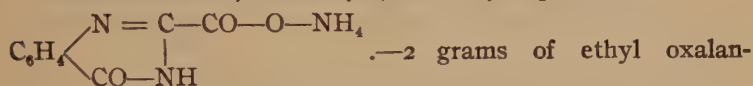


We should get a compound of a new naphtho tetrazine type. An effort was made to prepare this by the use of a dehydrating agent.

2.4 grams of 2-carbazino-3-amino-4-keto-dihydroquinazoline hydrochloride was treated as in the acetyl preparation. After filtering off the sodium chloride 2 grams of freshly fused zinc chloride was added to the acetic anhydride solution and the mixture evaporated to a small bulk. Water was then added and the evaporation continued to dryness on a water bath. The residue was then extracted with boiling benzol to eliminate the zinc chloride. There was thus obtained on concentrating the benzol extractions about 1.5 grams of a clear, brown syrup, very soluble in alcohol, chloroform, water, acetone, acetic acid, and methyl alcohol, and less readily soluble in benzol. No solvent could be found from which it could be obtained crystalline. After repeated attempts at purification by dissolving in different solvents, filtering and evaporating to dryness and drying at 110° , there was obtained a clear glass which was sticky at room temperature, but which could be readily pulverized at the temperature of ice and salt mixture. This melted to a clear brown liquid at $45-50^{\circ}$ (uncorr.). As

a last resort an attempt was made to distil this *in vacuo*, but as the heated vapor touched the bulb of thermometer, the bulb broke and the metallic mercury caused instant decomposition. The research was in too advanced a stage to permit time to make another preparation, so no analytical figures were secured. From its properties, however, it is an altogether different compound from the acetyl derivative.

Ammonium salt of 2-carboxyl-4-keto-dihydroquinazoline,

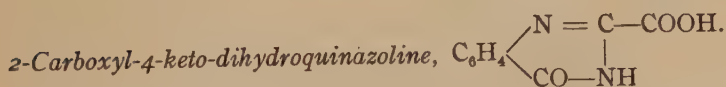


thranil were treated with a slight excess of ammonia in 95 per cent. alcohol. A reaction took place at once as was shown by the heat developed. At first the anthranil completely dissolved and was then suddenly precipitated again as a white powder. The mixture was warmed on a water bath, filtered, and washed several times with 95 per cent. alcohol.

Yield almost quantitative. The ammonium salt is a white crystalline powder only slightly soluble in alcohol and insoluble in benzol. It recrystallizes readily from hot water and long, silky needles, which melt at 229° (corr.) with evolution of gas (NH_3CO_2). For analysis it was repeatedly extracted with boiling alcohol and dried at 110° .

0.1380 gram gave 24 cc. nitrogen at 19° and 769 mm.

	Calculated for $\text{C}_9\text{H}_9\text{O}_3\text{N}_3$. Per cent.	Found. Per cent.
Nitrogen	20.28	20.26



—Griess²² describes a compound which he calls 4-keto-2-carboxyl-1.4-dihydro-1.3-benzdiazin and in which the double bond joins positions 2 and 3 rather than 1 and 2. He states that this is only slightly soluble in cold water or alcohol and

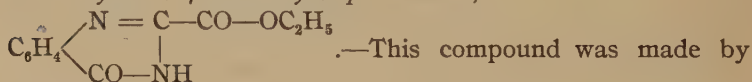
that on warming the solution or by treatment with acids it very easily loses CO_2 . No melting point or analysis is given.

The ammonium salt of 2-carboxyl-4-keto-dihydroquinazoline (see above) was hydrolyzed with cold concentrated hydrochloric acid and water added to precipitate the free acid, which was thrown down as a gelatinous mass. This was crystallized from dilute alcohol, melting constant on first recrystallization at 224° (corr.) with loss of CO_2 . It crystallizes from alcohol in which it is very soluble in white silky needles, very slightly soluble in benzol and almost insoluble in water. Unlike the acid described by Griess its solutions are perfectly stable and may be boiled with strong mineral acid without losing CO_2 .

0.0768 gram gave 10 cc. nitrogen at 23° and 770 mm.

	Calculated for $\text{C}_9\text{H}_8\text{O}_3\text{N}_2$. Per cent.	Found. Per cent.
Nitrogen	14.73	14.97

2-Ethyl-ester-4-keto-dihydroquinazoline,



two methods:

(1) A mixture of 1.5 grams ethyl oxalantranil and 0.42 gram urea were melted on an oil bath at 125° . The temperature was raised slowly to $140\text{--}150^\circ$ and maintained there for an hour. The melt was then allowed to cool and extracted with alcohol to separate any insoluble matter. From the alcohol extract on cooling a white, crystalline solid separated which was washed on the filter with water and dried.

(2) To an alcoholic solution of 0.33 gram urea 1 gram of ethyl oxalantranil was added and the mixture boiled for some time. This was then filtered and on cooling the same white crystalline compound was obtained as in (1).

2-Ethyl-ester-4-keto-dihydroquinazoline crystallizes from alcohol in tiny white needles which melt at 185.5° (corr.), are

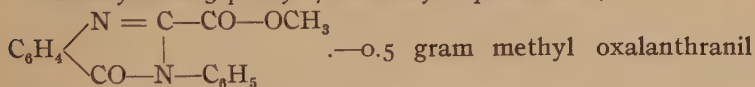
insoluble in water or in mineral acids, but dissolves readily in caustic alkali showing the enol structure. It is insoluble in strong sodium carbonate solution. When treated with aqueous ammonia, salt (see above) is obtained which is hydrolyzed by strong hydrochloric acid to 2-carboxyl-4-ketodihydroquinazoline, melting at 224° . (See above). For analysis the ester was recrystallized from 95 per cent. alcohol and dried at 110° .

0.2419 gram substance gave 27.4 cc. nitrogen at 22 and 764 mm.

	Calculated for $C_{11}H_{10}O_3N_2$. Per cent.	Found. Per cent.
Nitrogen	12.83	12.90

The presence of the ester group was proven by iodoform tests.

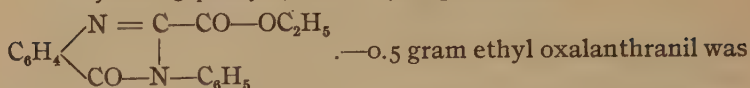
2-Methyl-ester-3-phenyl-4-keto-dihydroquinazoline,



was treated with a slight excess of anilin and the mixture heated over a free flame until the reaction began. As soon as boiling commenced the flame was removed and the reaction allowed to proceed. Water was given off as was shown by the crackling of the fused mixture. On cooling, the mass solidified. This was extracted with dilute alcohol from which on cooling small, white flakes separated, melting constant on recrystallization at 203.5° (corr.). These become soft at about 120° . Yield very poor. The ester is very soluble in alcohol and almost insoluble in water. For analysis it was recrystallized from dilute alcohol and dried at 110° .

0.1218 gram gave 10.6 cc. nitrogen at 23° and 758 mm.

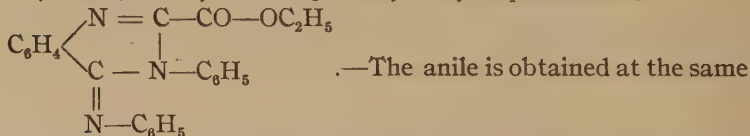
	Calculated for $C_{16}H_{12}O_3N_2$. Per cent.	Found. Per cent.
Nitrogen	10.00	9.78

2-Ethylester-3-phenyl-4-keto-dihydroquinazoline,

heated for a moment with an excess of anilin and the mass cooled. This was then extracted with 95 per cent. alcohol, which upon cooling deposited the ethyl ester in beautiful white plates melting at 160° (corr.) and constant on recrystallization. The ester is insoluble in cold KOH but dissolves on heating. It is not saponified by concentrated hydrochloric acid on boiling. It is readily soluble in alcohol, but almost insoluble in water.

0.1482 gram gave 11.8 cc. nitrogen at 15° and 566 mm.

	Calculated for $\text{C}_{17}\text{H}_{14}\text{O}_2\text{N}_2$ Per cent.	Found. Per cent.
Nitrogen	9.50	9.40

4-Anile, 2-Ethyl Ester, 3-Phenyl-dihydroquinazoline,

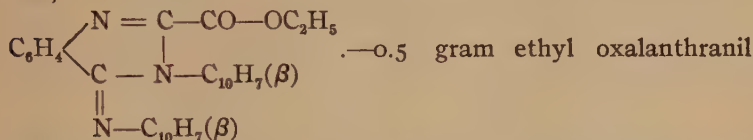
time as the ethyl ester above described by heating ethyl oxalanthranil with an excess of anilin. If the heating is continued for several minutes the anile is obtained in good yield. It is separated from the keto ester by its insolubility in alcohol. The anile is a white, crystalline powder, insoluble in water, alcohol, benzol, or ordinary organic solvents, and melting with effervescence at 291° (corr.). For analysis it was repeatedly extracted with boiling alcohol and dried at 110° .

0.1450 gram gave 14.6 cc. nitrogen at 22° and 759 mm.

	Calculated for $\text{C}_{23}\text{H}_{19}\text{O}_2\text{N}_3$ Per cent.	Found. Per cent.
Nitrogen	11.36	11.40

A similar insoluble compound was obtained from the methyl ester condensation but not in quantities sufficient for analysis.

2-Ethyl-ester-3-β-naphthyl-4-β-naphthylimino-dihydroquinazoline,

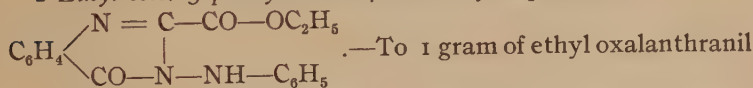


was mixed in a mortar with 0.5 gram β-naphthylamine and the mixture then melted in a small flask in an oil bath. When the contents of the flask had completely liquefied, the heat was raised until boiling began. The mixture when cold was extracted with 95 per cent. alcohol. The condensation product is a grayish-white crystalline powder, insoluble in alcohol, acetone, amyl alcohol, benzol, or water, and melting to an amber liquid at 253°-4° (corr.). For analysis it was repeatedly extracted with hot alcohol and dried at 110°.

0.1284 gram gave 9.6 cc. nitrogen at 16° and 770 mm.

	Calculated for $\text{C}_{31}\text{H}_{23}\text{O}_2\text{N}_3$.	Found.
	Per cent.	Per cent.
Nitrogen	8.95	8.83

2-Ethyl-ester-3-phenylamino-4-keto-dihydroquinazoline,



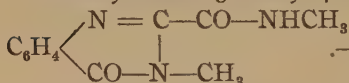
was added an equal molecular quantity of phenylhydrazine and the mixture heated over a free flame. This was then heated to boiling, water was split out by the reaction, as was shown by the crackling and condensation of water on the upper portion of the tube. No odor of alcohol was obtained. On cooling the melt solidified to a clear amber glass. This was dissolved in hot alcohol and allowed to crystallize. The crystals so obtained were pressed out on a suction filter and thoroughly washed with dilute alcohol. On redissolving in

a large volume of alcohol and allowing to stand 48 hours, long lemon-yellow needles separated, melting at 142° (corr.) to a clear amber liquid. The quinazoline is insoluble in water, but soluble in alcohol, benzol and acetone, with a bright yellow color; insoluble in dilute mineral acid; insoluble in cold alkali but dissolving on heating.

0.1478 gram substance gave 17.6 cc. N at 20° and 762 mm.

	Calculated for $C_{17}H_{15}O_2N_3$ Per cent.	Found. Per cent.
N	13.58	13.65

2-Methyl-amide-3-methyl-4-keto-dihydroquinazoline,



—One gram of ethyl oxalanthranil

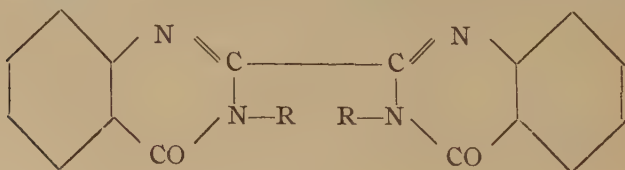
was added to a slight dimolecular excess of an aqueous solution of methyl amine. The solution so obtained was evaporated to a small bulk from which, on long standing, beautiful prismatic crystals separated, much resembling crystals of pink quartz. These crystals are very soluble in water and soluble to a much less extent in alcohol. They melt sharply at 160° (corr.).

0.1100 gram gave 18 cc. N at 14.5° and 774 mm.

	Calculated for $C_{11}H_{11}O_2N_3$ Per cent.	Found. Per cent.
N	19.35	19.51

IV. Condensation of Oxaldianthranil.

By the action of a primary amine upon oxaldianthranil we should be able to prepare diquinazolonyls of the type



where R is an aromatic or alkyl radicle, according to the primary amine used. The reaction, however, does not go in this manner, and up to the present writing no satisfactory graphic formulae have been found which would agree with the analysis of the compounds obtained. Only a few of the compounds were analyzed completely, for after it was seen from a few instances that the reaction did not go as intended, the study was changed to more promising fields. A short résumé of the results obtained is, however, not without value

Condensation of Hydrazine Hydrate with Oxaldianthranil.—Two grams of oxaldianthranil were treated with a slight excess (two molecules) of hydrazine hydrate in alcoholic solution and heated to boiling. The reaction mixture was allowed to stand twelve hours and then filtered and the insoluble mass of tiny white crystals washed with alcohol and dried at 110° . Yield 2.2 grams. The product so obtained is white, crystalline, insoluble in alcohol, acetone, ether, amyl alcohol, benzol, chloroform, ligroin, or methyl alcohol; somewhat soluble in acetic acid, very dilute hydrochloric acid and strong (1:1) KOH; insoluble in sodium carbonate solution, and melting at 241° (corr.)

0.1565 gram gave 31.4 cc. N at 23° and 768 mm.

(1) 0.1147 gram gave 0.2200 gram CO_2 (water lost by acidant).

(2) 0.1879 gram gave 0.3652 gram CO_2 and 0.0780 gram H_2O .

	Per cent.	Found.	Per cent.
N	22.85		...
C	52.31		52.50
C	4.65		...

When boiled with acetic anhydride a diacetyl derivative is evidently formed, which is white, amorphous, insoluble in glacial acetic acid or acetic anhydride, alcohol, nitrobenzol, benzol, or anilin, and decomposing at 300° (uncorr.).

0.1240 gram gave 20.6 cc. N at 22.5° and 764 mm.

Nitrogen found = 18.87 per cent.

The above analysis approximates a formula of $C_{16}H_{10}O_5N_6$ and a diacetyl $C_{20}H_{20}O_7N_8$.

	Calculated. Per cent.
N	22.58
C	51.61
H	4.27
N (acetyl)	18.40

The discrepancy might be accounted for in the insolubility of each compound and the inability of being sure of its purity. However, no graphic formula has as yet been found which will appear probable.

Condensation of Oxaldianthranil with Semicarbazid.—One and five-tenths grams dianthranil was treated with slightly more than two molecules of semicarbazid and the mixture heated to boiling. By this method two products were obtained, one melting with decomposition at 330° (uncorr.), which was not further investigated. From the alcoholic extract a white powder separated, melting on recrystallization at 224° (corr.), soluble in alcohol, benzol, and acetic acid.

0.0870 gram gave 6.2 cc. nitrogen at 22.5° and 767 mm.

	Found. Per cent.
N	8.13

Condensation of Oxaldianthranil with Anilin.—The dianthranil was treated with an excess of anilin heated to boiling in an oil bath and the crude product extracted with acetic acid. Two products were thus obtained, one soluble in acetic acid and one insoluble. The soluble portion was recrystallized from glacial acetic acid. Melting point 258° (uncorr.), only slightly soluble in acetic acid, and almost insoluble in other solvents excepting anilin or nitrobenzol. Yield too small for analysis. The insoluble portion melts with decomposition at 310° (uncorr.) and forms small white shiny crystals.

0.1321 gram gave 13.4 cc. N at 14° and 770 mm.

	Found. Per cent.
N	12.09

Condensation of Oxaldianthranil with Ammonia.—Oxaldianthranil was condensed with ammonia in alcoholic solution. The resulting product was washed with water and dried. It forms a white, crystalline solid, melting at 316–317° (corr.) with evolution of gas, and insoluble in organic solvents, including alcohol, benzol, acetone, chloroform, ligroin, amyl alcohol and acetic acid. That it is not the quinazoline compound is shown by the fact that it will not dissolve in dilute alkali even on heating, thus showing the absence of the enol structure.

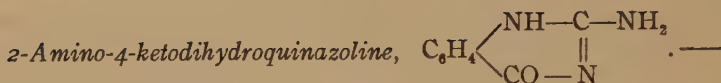
0.1810 gram gave 20 cc. N at 22° and 751 mm.

	Found Per cent.
N	12.37

V. Other Condensations.

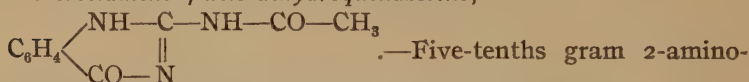
2-Ethoxy-4-ketodihydroquinazoline. $\text{C}_6\text{H}_4 \begin{cases} \text{NH}-\text{C}-\text{O}-\text{C}_2\text{H}_5 \\ \text{CO}-\text{N} \end{cases}$

—This compound was prepared as described by Griess.¹ Twenty grams anthranilic acid was dissolved in 800 cc. 95 per cent. alcohol, and this solution saturated with dicyanogen by passing cyanogen gas through the solution for three hours. The liquid was then a light yellow color, which upon standing for eight days had turned to a dark brown. At the end of eight days the solution was filtered from any insoluble residue, concentrated to a small bulk, and allowed to crystallize. The crystals so obtained were boneblackened and recrystallized from alcohol. Yield 15 grams. The quinazoline forms feathery tufts of crystals, melting at 176° (corr.), insoluble in water or sodium carbonate, readily soluble in hot alcohol.



This was prepared from the above ethoxy compound as described by Griess.- Fourteen grams 2-ethoxy-4-ketodihydroquinazoline were treated with strong alcoholic ammonia in a sealed tube for forty hours at 100–110°. On opening the tube a mass of beautiful iridescent crystals was obtained, which upon washing with dilute alcohol were pure. Yield 9 grams. The quinazoline forms coarse needles, insoluble in water, only very slightly soluble in alcohol, soluble in strong KOH, and soluble in acetic anhydride to form an acetyl derivative. The aminoquinazoline does not melt below 300°. All attempts to diazotize the amino group were unavailing, as no diazotization took place even on boiling.

2-Acetamino-4-keto-dihydroquinazoline,

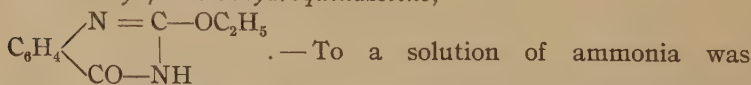


4-keto-dihydroquinazoline was treated with acetic anhydride in excess. Instantly the transparent crystals (previously dried at 110°) became chalky and lost their crystalline structure. On warming this the chalky mass slowly dissolved. The solution was boiled several minutes and, on cooling, long silky needles separated. Very slightly soluble in alcohol, but easily recrystallized from glacial acetic acid. Melting point 273.5° (corr.).

0.1320 gram gave 23.3 cc. N at 20° and 762 mm.

	Calculated for $\text{C}_{10}\text{H}_9\text{O}_2\text{N}_3$. Per cent.	Found. Per cent.
N	20.69	20.24

2-Ethoxy-4-keto-dihydroquinazoline,



added a portion of ethyl ester anthranil. A white solid sepa-

rated at once. The solution was warmed, filtered, and the solid recrystallized from alcohol. The quinazoline forms beautiful white needles somewhat soluble in hot water, insoluble in sodium carbonate solution, soluble in hot alkali (probably with saponification) and very soluble in alcohol, melting at 153–154° (corr.).

0.1212 gram substance gave 15.7 cc. N at 22° and 762 mm.

	Calculated for $C_{10}H_{10}O_2N_2$ Per cent.	Found. Per cent.
N	14.73	14.71

This compound is decidedly different from the one described by Griess (see above), but the difference is probably accounted for by the different position of the double bond in the nucleus.

Ammonia on 2-Ethoxy-4-keto-2,4-dihydroquinazoline.—Eight-tenths gram 2-ethoxy-4-keto-dihydroquinazoline (melting point 153–154°) (corr.) was heated in a sealed tube at 150–170° with alcoholic ammonia for seven hours. Upon opening the tube a mass of white glistening needles was found. These were filtered, washed with water and alcohol, and dried at 110°. Yield 0.5 gram. The same compound may be obtained by dissolving ethyl ester anthranil in strong ammonia and warming for some time on a water bath. The yield, however, is less than that obtained by the sealed tube method. The condensation product forms long, colorless, coarse needles, almost insoluble in water, alcohol, benzol, acetic acid, dilute mineral acids or alkalies, and melts above 335°. The product separating from the acetic anhydride solution in which the original product was slightly soluble, melts above 335° and was not further investigated. No change was produced by boiling the condensation product in a dilute hydrochloric acid solution with sodium nitrite.

0.1393 gram gave 38.6 cc. N at 17° and 764 mm.

(1) Analysis of sealed tube product: 0.1224 gram gave 0.2631 gram CO_2 and 0.0429 gram H_2O .

(2) Analysis of ammonia on water bath product: 0.1471 gram gave 0.3128 gram CO_2 and 0.0504 gram H_2O .

	Found.	
	Per cent.	Per cent.
N	32.33	...
C	58.69	58.24
H	3.92	3.84

Oxygen by difference, 5.33 per cent.

These analyses approximate a formula of $(\text{C}_{15}\text{H}_{12}\text{ON}_7)_x$ but no graphic formula has been devised.

	Calculated.
	Per cent.
C	58.82
H	3.88
N	32.02
O	5.22

RÉSUMÉ.

1. The esters of oxalanthranilic acid may be obtained by heating one molecule of oxal ester with one molecule of anthranilic acid.

2. These esters are converted into the corresponding anthranils by boiling with acetic anhydride.

3. By the action of one molecule of oxal ester upon two molecules of anthranilic acid and treating the oxaldianthranilic acid so formed with acetic anhydride oxaldianthranil is obtained.

4. By the action of ethyl chlorformate upon anthranilic acid, anthranilic acid ethylformate is obtained, which, when treated with acetic anhydride gives the corresponding ethyl ester anthranil.

5. By the action of primary amines upon various anthranils there have been obtained certain substituted quinazolines.

6. By the synthesis of the oxalanthranils and subsequent treatment with primary amines the formation of substituted 2-carboxyl-4-keto-dihydroquinazolines has been made possible.

7. Hydrazine hydrate acting upon acetanthranil forms 2-methyl-3-*N*-amino-4-ketodihydroquinazoline, which is of interest owing to the *N*-amino group.

8. By the action of nitrous acid the *N*-amino group is replaced by hydrogen.

9. The *N*-amino body will not condense with ketones but condensation takes place readily with benzaldehyde.

10. By the action of phenyl-isocyanate upon 2-methyl-3-*N*-amine-4-ketodihydroquinazoline the corresponding phenyl uramino derivative is formed.

11. By the action of nitrous acid and subsequent "coupling" with α - and β -naphthol, 2-methyl-3-*N*-amino-4-ketodihydroquinazoline gives dye stuffs of unknown structure.

12. Oxaldianthranil condenses with primary amines to

form compounds for which as yet no graphic formulae have been devised.

13. 2-Amino-4-ketodihydroquinazoline (Griess) will not diazotize even at 100° , but readily forms a monoacetyl derivative.

14. By treating ethyl ester anthranil with ammonia a new 2-ethoxy-4-ketodihydroquinazoline is obtained.

15. When this compound was treated with ammonia a compound of unknown structure resulted.

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BIOGRAPHICAL.

Ross Aiken Gortner was born near O'Neill, Holt County, Nebraska, March 20th, 1885. He entered Nebraska Wesleyan University as a sub-Freshman in the fall of 1902, and received the degree of Bachelor of Science in June, 1907. During 1906-07 he held the position of Research Assistant in Agricultural Chemistry at the University of Nebraska. In the spring of 1907 he was appointed James M. Goewey Scholar in Chemistry at the University of California for 1907-08, but later resigned this to take the position of Assistant in Chemistry, Faculty of Arts, at the University of Toronto, where he received the degree of Master of Arts, in June, 1908. Having been appointed University Fellow in Chemistry he entered Columbia University in the fall of 1908 and studied for the degree of Doctor of Philosophy.

Major subject, organic chemistry.

Minors, physical chemistry and physiological chemistry.

Fellow of the London Chemical Society.

Member of the American Chemical Society.

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